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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/849,969	05/08/2001	Randolph J. Noelle	037003-0280613	1327

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EXAMINER	
GAMBEL, PHILLIP	
ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 05/04/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/849,969	NOELLE, RANDOLPH J.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *8/15/05; 9/15/05*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5-10,12-14,17 and 19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5-10,12-14,17 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 CFR 1.114.
Applicant's submission filed on 9/15/05 has been entered.

Applicant's amendment, filed 8/15/05, has been entered.
Claims 1, 12, 17 and 19 have been amended.

Claims 1, 5-10, 12-14, 17 and 19 are pending and being acted upon presently.

Claims 2-4, 11, 15-16, 18 and 20-21 have been canceled previously.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.
This Action will be in response to applicant's arguments in the amendment, filed 8/15/05.
The rejections of record can be found in the previous Office Action.

3. Claims 12-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 12-14 are indefinite in the recitation of "T cell mediated autoimmune responses associated with type I diabetes" in that the nature or parameters of said "autoimmune responses are ill-defined and ambiguous.

Applicant's arguments, filed 8/15/05, have been fully considered but are not found convincing essentially for the reasons of record.

Applicant argues in conjunction with various Exhibits that as of the earliest filing date, T cell mediated autoimmune responses associated with type I diabetes were well known.

While insulitis and pancreatic beta cell /islet cell destruction were well known characteristics of type I diabetes, neither the specification nor applicant's Exhibits fail to particularly point out and distinctly claim the subject matter which applicant regards as the invention. For example, the metes and bounds of the claimed "responses" are ambiguous in which parameters (e.g. the nature and type cytokine or T cell regulation) are being relied upon.

For example, the molecular nature of the putative immunogenic signals involved in the autoimmune response of IDDM is unknown (e.g. see page 616, Autoimmune Diabetes: A TH1-Cell –Mediated Immune Process and Immunostimulatory Procedures Prevent IDDM: Correction of a Cytokine Balance? on pages 616-619, including page 616, column 2, paragraph 1 of Rabinovitch, Diabetes 43: 613-621, 1994).

Again, applicant is invited to amend the claims to recite specific endpoints that can be measured.

Applicant should specifically point out the support for any amendments made to the disclosure.
See MPEP 714.02 and 2163.06

4. The previous rejection under 35 U.S.C. § 112, first paragraph, written description / new matter with respect to the recitation of "wherein the tissue destruction results from a T cell-mediated immune reaction to one or more autoantigens" has been withdrawn in view of applicant's amended claims, filed 8/15/05.

5. Claims 1, 5-10, 17, and 19 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. The specification as originally filed does not provide support for the invention as now claimed:
"wherein the anti-gp39 antibody or fragment binds to an epitope which is specifically bound by a monoclonal antibody produced by the 24-31 hybridoma".

Applicant's arguments, filed 8/15/05, have been fully considered but are not found convincing essentially for the reasons of record.

Applicant's amendment, filed 8/15/05, submits that the subgenus of 24-31 antibody epitopic specific was described in the application as file (e.g. see pages 4-6 of the instant specification) and that a subgenus having that specificity was inherently or impliedly, if not explicitly, described given this well known technology.

It appears that applicant acknowledges that these particular "phrase" does not have written description in the specification as filed; therefore the claims represent a departure from the specification and claims as originally filed.

Here again, applicant's reliance on generic disclosure of anti-gp39 antibodies (see pages 4-6 of the specification) and a single species of anti-gp39 antibodies produced by the 24-31 hybridoma (see page 6, paragraph 2 of the instant specification) do/does not provide sufficient direction and guidance to the features of establishing a new subgenus "an 24-31 antibody epitopic specificity", as currently claimed

It is noted that a generic or a sub-generic disclosure cannot support a species unless the species is specifically described. It cannot be said that a subgenus is necessarily described by a genus encompassing it and a species upon which it reads. See In re Smith 173 USPQ 679, 683 (CCPA 1972) and MPEP 2163.05.

Obviousness is not the standard for the addition new limitations to the disclosure as filed. It is noted that entitlement to a filing date does not extend to subject matter which is not disclosed, but would be obvious over what is expressly disclosed. Lockwood v. American Airlines Inc., 41 USPQ2d 1961 (Fed. Cir. 1977).

The specification as filed does not provide a sufficient written description of specific "limitations" within this newly submitted phrase. The specification does not provide sufficient blazemarks nor direction for the instant methods encompassing the above-mentioned "limitations" as currently recited. The instant claims now recite limitations which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed.

Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the new matter in the response to this Office Action

Alternatively, applicant is invited to provide sufficient written support for the "limitations" indicated above. See MPEP 714.02 and 2163.06

Applicant's comments concerning the enablement of chimeric and humanized antibodies by early 1992 are acknowledged,

However, as applicant also acknowledges,

This is a separate issue of enablement, while the rejection of record and maintained herein is one of written description / enablement.

Applicant is reminded that Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, 1115 (CAFC 1991) makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

6. New Ground of Rejection

Claims 12-14 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention

It is well established in the art that the formation of an intact antigen-binding site generally requires the association of the complete heavy and light chain variable regions of a given antibody, each of which consists of three CDRs which provide the majority of the contact residues for the binding of the antibody to its target epitope. The amino acid sequences and conformations of each of the heavy and light chain CDRs are critical in maintaining the antigen binding specificity and affinity which is characteristic of the parent immunoglobulin. It is expected that all of the heavy and light chain CDRs in their proper order and in the context of framework sequences which maintain their required conformation, are required in order to produce a protein having antigen-binding function and that proper association of heavy and light chain variable regions is required in order to form functional antigen binding sites.

For example, even minor changes in the amino acid sequences of the heavy and light variable regions, particularly in the CDRs, may dramatically affect antigen-binding function as evidenced by Rudikoff et al (Proc Natl Acad Sci USA 79: 1979- 1983,1982). Rudikoff et al. teach that the alteration of a single amino acid in the CDR of a phosphocholine-binding myeloma protein resulted in the loss of antigen-binding function.

It is unlikely that fusion proteins as defined by the claims which may contain less than the full complement of CDRs from the heavy and light chain variable regions of an gp39-/CD40L-specific antibody in unspecified order and fused to any human or nonhuman framework sequence, have the required binding and inhibitory functions to prevent T cell mediated immune responses / tissue destruction.

The specification provides insufficient direction or guidance regarding how to produce fusion proteins and antibodies as broadly defined by the claims. Undue experimentation would be required to produce the invention commensurate with the scope of the claims from the written disclosure alone. Further, the specification does not teach that a functional humanize antibody can be obtained by replacing the CDR regions of an acceptor antibody with the CDRs of a donor antibody. As evidenced by Adair et al. (US Patent 6,632,927) transfer of CDR regions alone are often not sufficient to provide satisfactory binding activity in the CDR-grafted product (see column 2, lines 58-61).

Therefore, in view of the lack of guidance in the specification and in view of the discussion above one of skill in the art would be required to perform undue experimentation in order to practice the claimed invention

Applicant is invited to amend the claims to provide for a functional gp39-specific / CD40L-specific antibodies that can prevent T cell mediated immune responses / tissue destruction, encompassed by the claimed methods.

7. For examination purposes, the claims can be read on preventing the elaboration of T cell mediated tissue destruction / autoimmune responses associated with type I diabetes as part of a therapeutic regimen during the treatment of type I diabetes rather than being limited to preventing type I diabetes per se.

8. Claims 1, 5-10, 12-14, 17 and 19 are rejected under 35 U.S.C.§ 103(a) as being unpatentable Lederman et al. (U.S. Patent No. 6,592,868) in view of Noelle et al. (U.S. Patent No. 5,747,037) for the reasons of record.

Applicant's arguments have been fully considered but are not found convincing essentially for the reasons of record.

Applicant's arguments and the examiner's rebuttal are essentially the same of record.

Although the 5c8 antibody and the instant 24-31 antibody epitope specificities nor describe "T cell mediated autoimmune responses" per se,
the prior art , including both Lederman et al. and Noelle et al. clearly provided for inhibiting cell-mediated inflammatory conditions, autoimmunity or diabetes at the time the invention was made with 5C8-specific / CD40L-specific antibodies.
The prior art teaching of Lederman et al. is not limited to treating B cell immune responses only, given its teaching of inhibiting transplant rejection and autoimmune diseases such as diabetes.

Although applicant argues that there is no suggestion in the '037 in merely administering the gp39 antagonist without antigen,
Lederman et al. does teach treating diabetes with 5c8- (gp39-, CD40 ligand-) specific antibodies in the absence of antigen presenting cells.
In addition, autoimmunity by its very nature encompasses the presence of autoantigen.
'037 provides for a more efficient method for inducing long term specific nonresponsiveness to autoantigens by providing antigen presenting cells in methods to treat an autoimmune condition such as diabetes, already taught to be treated with CD40 ligand-specific antibodies in the absence of antigen presenting cells by Lederman et al.
Further, it is noted that the claimed methods recite "comprising" which leaves the claim open for the inclusion of unspecified ingredients even in major amounts. See MPEP 2111.03.

Given the assertions of unexpected results, the prior art already provides clear direction in providing for the particular 24-31 CD40 ligand-specific antibody in the treatment of diabetes at the time the invention was made.

In this case the teachings of both the primary and second references indicate success in treating diabetic patients with anti-CD40 ligand antibodies in the face of having to solve the same or nearly the same problem would have led one of ordinary skill in the art at the time the invention was made to combine the references to treat the same or nearly the same diabetic patient populations with antagonistic therapeutic anti-CD40 ligand antibodies to dampen the well known inflammatory problems associated with diabetic patients in the art.

The strongest rationale for combining reference is a recognition, expressly or implicitly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent that some advantage or expected beneficial result would have been produced by their combination In re Sernaker 17 USPQ 1, 5-6 (Fed. Cir. 1983). See MPEP 2144.

In response to applicant's arguments against the references individually, one cannot show non-obviousness by attacking references individually where the rejections are based on combinations of references. In re Keller , 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., Inc. , 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). See MPEP 2145.

Applicant's assertions of unexpected results do not overcome clear evidence of obviousness of treating patients with diabetes with anti-CD40 ligand antibodies, including the 24-31 antibody at the time the invention was made

As pointed out previously, although Lederman is silent about the prevention of a T cell mediated autoimmune response associated with type I diabetes, it does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure. See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d 1508 (CAFC 2001).

"{i}t is a general rule that merely discovering and claiming a new benefit of an old process cannot render the process again patentable. "In re Woodruff, 16 USPQ2d 1934, 1936 (Fed. Cir. 1990). The mechanism of action does not have a bearing on the patentability of the invention if the invention was already known or obvious. Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. In re Wiseman, 201 USPQ 658 (CCPA 1979). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See MPEP 2145.

Given the antagonistic properties of the particular 24-31 and 89-76 CD40L-specific antibodies taught by Noelle et al. ('037), the ordinary artisan would have been motivated to substitute these CD40L antagonists into the methods of treating autoimmune diseases such as diabetes, as taught by Lederman, given their inhibitory properties were consistent with the antagonistic CD40L-specific antibodies taught by the prior art. Noelle et al. ('037) and Lederman et al. all teach the advantages of anti-CD40L antibodies to inhibit immune responses by targeting the CD40L on T helper cells in therapeutic modalities of immunosuppression at the time the invention was made. Appliant's arguments that the prior art, including Lederman et al. are only limited to treating B cell immune response only is not consistent with the a reasonable interpretation of the prior art in the applicability of CD40L-specific antibodies in the treatment of various inflammatory or immune regulated conditions and disorders, including diabetes itself.

While the prior art anti-CD40L antibodies may have been tested with respect to parameters associated with B cell activation and immunoglobulin production, the prior art clearly teaches that CD40L was expressed on important activated CD4+ T cells that regulated various immune responses and that CD40L was targeted in conditions and disorders known to be cell-mediated at the time the invention was made.

From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments are not found persuasive.

9. No claim allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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